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09/902,713	07/10/2001	Avi Ashkenazi	10466/71	1320

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	23

DATE MAILED: 06/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/902,713	Applicant(s) ASHKENAZI ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 March 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *21* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 3/31/03 (Paper No. 17), is acknowledged.
Claim 44 has been cancelled. Claims 1-38 have been cancelled previously.
Claim 39 has been amended.
Claims 39-43 are pending and are under consideration in the instant application.

2. This Office Action will be in response to applicant's arguments, filed 3/31/03 (Paper No. 17). The rejections of record can be found in the previous Office Action (Paper No. 11).

It is noted that New Grounds of Rejection are set forth herein.

3. Applicant's cancellation of claim 44 has obviated the previous objections and rejections with respect to this claim.

Objections not reiterated may be considered obviated by Applicant's amendment, filed 3/31/03.

Drawings

4. The formal drawings filed 3/31/03 have been found acceptable by the Draftsman.

Priority

5. Applicant's comments, filed 3/31/03, regarding the priority claimed in the instant application are acknowledged.

Applicant argues that the claims as amended do have a specific and substantial utility and therefore are entitled to an effective filing date of Feb. 11, 2000 because the results providing utility were first disclosed in PCT/US00/03565.

For the reasons addressed in detail below in the rejections under 35 USC 101, Applicant's arguments that the invention as now claimed has a specific and substantial utility are not found convincing. It is further noted that priority requires adequate written description under 35 USC 112.

Accordingly, the subject matter defined in claims 39-43 appears to have an effective filing date of 7/12/01.

IDS

6. Applicant's supplemental IDS, filed 3/31/03, is acknowledged. With the exception of the Blast Results, these references on the PTO-1449 filed 3/31/03 appear to be duplicates of the references provided with Paper No. 11. Accordingly they have been considered, as indicated by initialing, but lined through as duplicate citations.

As previously noted in Paper No. 11, the Blast results fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the sequence alignments provided fail to provide any of the relevant information with respect to publisher, author (if any), title, relevant pages of the publication, date, and place of publication with respect to the sequences compared.

Claim Objections

7. Claim 43 stands objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, claim 39. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form.

Applicant argues in the response filed 3/31/03 that "labeled antibody" is found in the specification on page 77 at lines 9-12. However, at issue is whether the addition of a label broadens the scope of the subject matter encompassed by the term "antibody". Since "antibody is not defined as encompassing labels; the recitation that the antibody is "labeled" fails to further limit the "antibody" recited in claim 39.

It is again suggested that Applicant rewrite the claim in independent form.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. § 101 reads as follows:

> *"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".*

9. Claims 39-43 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Applicant's arguments with respect to the asserted utility of PRO269 as a diagnostic marker for lung cancer, filed 3/31/03, have been fully considered but have not been found convincing.

The rejection of record in full may be found in Paper No. 11. The asserted utility of a diagnostic marker for lung tumors does not appear to affect the Examiner's previous comments with respect to other asserted utilities, which may be found in full in Paper No. 11.

Applicant argues in the Remarks filed 3/31/03 that PRO269 showed approximately 2-3 fold amplification in 8 primary lung tumors. Applicant asserts that an antibody to PRO269 therefore has a specific, substantial and credible use as a diagnostic reagent for lung cancer.

Applicant provides in support of this assertion a Declaration under 37 CFR 1.132 by Dr. Goddard supporting that the TaqMan PCR technique is technically sensitive enough to detect at least a 2-fold increase in gene copy number relative to control. Dr. Goddard concludes that a gene identified as being amplified at least 2-fold by the quantitative TaqMan PCR assay in a tumor sample relative to a normal sample is useful as a marker for the diagnosis of cancer, for monitoring cancer development and/or for measuring the efficacy of cancer therapy.

It is noted that a second, unexecuted Declaration under 37 CFR 1.132 by Dr. Goddard was also filed on 3/31/03. Since the Declaration was not executed, statements therein cannot be found convincing. However, it is noted that similar arguments are advanced, but 4-fold, rather than 2-fold amplification of a gene is described as "significant".

As discussed in Applicant's Remarks filed 3/31/03, a 2 fold amplification corresponds to a ΔCt value of 1 unit. ΔCt values of 2 units correspond to a 4-fold amplification.

While the Examiner acknowledges that the results shown in Table 9 do show that the PRO269 gene had a ΔCt value of above 1 in 8 primary lung tumors, the PRO269 gene was not detected in 9 other primary lung tumors. In addition, the ΔCt values for the PRO269 gene were all less than 2 units, and most were close to 1 ΔCt. It appears form the discussion on page 22 of the disclosure (e.g., lines 11-32) that a CT value of +/- 1 identifies "background" of normal human DNA compared to the test DNA. Thus the significance of a ΔCt that close to 1 is far from clear.

Further, the amplification assays do not appear to control for aneuploidy. The data do not appear to be supported by analysis of mRNA or protein expression. A slight amplification of a gene in a cancer tissue does not necessarily mean that the gene is overexpressed: rather it may simply indicate that the cancer tissue is aneuploid (see e.g., Sen Curr. Opin. Oncol. 2000; 12:82-88).

Thus in view of ΔCt values that are only slightly above 1, the absence of any signal in as many primary lung tumors as were found to have a ΔCt above 1, and the absence of appropriate controls for the aneuploidy of the samples; the totality of the evidence does not support Applicant's assertion that one of skill in the art would find it more likely than not that PRO269 was a diagnostic marker for lung cancer.

The Examiner therefore maintains that at present the instant disclosure fails to clearly establish how one of skill in the art could use the claimed invention in a way that constitutes a credible specific and substantial utility. The disclosed modest increase of gene expression in a limited number of lung tumors for which aneuploidy was not assessed appears only to provide a starting point for further research and investigation into potential practical uses of the claimed PRO269 gene.

In addition, the instant claims are drawn to an antibody, rather than a gene. Even were a diagnostic utility established for the gene, it is unclear whether a specific and substantial utility for the antibody would follow, particular in the absence of data supporting overexpression of the gene to produce a protein product that could be detected by the antibody reagent.

The rejection is therefore maintained for the reasons of record set forth in full in Paper No. 11.

Applicant is again directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 39-43 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments, filed 3/31/03, and the Examiner's comment with respect to the amended claims and the asserted utility of PRO269 as a diagnostic marker for lung cancer and the asserted utility of the antibody to PRO269 as a diagnostic reagent have been addressed supra.

The rejection is therefore maintained for the reasons of record set forth in full in Paper No. 11.

12. The antibody to the PRO269 polypeptide of SEQ ID NO:96 itself does not appear to be enabled for the reasons set forth supra. However, even were sufficient objective evidence provided that an antibody to the PRO269 polypeptide of SEQ ID NO:96 were enabled for one or more of the asserted uses, the following rejections would still apply:

Claims 39-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

Applicant has argued in the response filed 3/31/03 that antibodies to PRO269 may be used as diagnostic reagents.

As noted supra, diagnostic applications also require guidance that the protein detected is either differentially expressed or overexpressed in a particular condition. However, the specification does not appear to establish the expression patterns of the PRO269 polypeptide. Thus undue experimentation of the skilled artisan would be required to identify conditions in which expression of PRO269 was altered so that an anti-PRO269 antibody could be used diagnostically.

Thus given the absence of working examples and the insufficient guidance with respect to situations in which the skilled artisan could use the PRO269 antibody; the Examiner maintains that it would require extensive and undue experimentation to of the skilled artisan to use the instant PRO269 antibodies.

The rejection is therefore maintained for the reasons of record set forth in full in Paper No. 11.

13. Applicant's amendment, filed 3/31/03, has obviated the previous rejection of claims 39-43 under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim Rejections – 35 U.S.C. § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 39-43 are rejected under 35 U.S.C. 102(b), *or in the alternative under 35 U.S.C. 102(a)*, as being anticipated by Wood et al. (WO 99/14328, see pages 1, 12, 39, 56, 72, 83-85, 92-98, 101, 108-112, 126-127, 185-187, Figures 35 and 36, of record), as evidenced by the attached alignments "D" (of record).

Applicant's arguments, filed 3/31/03, have been fully considered but have not been found convincing.

Applicant' argues that the instant claims are entitled to an effective filing date of February 11, 2000.

For the reasons set forth supra, Applicant's argument with respect to the effective filing date of the instant claims has not been found convincing.

Applicant also argues that In re Wilder 166 USPQ 545 (C.C.P.A. 1970) invalidates Wood et al. as a reference because the polypeptide bound by the instantly recited antibody has properties completely different from those attributed to the polypeptide by Wood et al.

However, a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

It is noted that the Court in In re Wilder also appreciated that when the identical compound was described in the prior art, the evidence "quite reasonably also permits the inference that the reference patentee might only have been unaware of a particular property of the compound he did disclose. Such proof clearly falls short of defeating a case of anticipation." In re Wilder 166 USPQ 545, 549 (C.C.P.A. 1970).

As previously noted, Wood et al. teach an isolated PRO269 polypeptide having 100% amino acid sequence identity to SEQ ID NO:96 as shown in Figure 36 of the instant application, as evidenced by the attached alignment.

Wood et al. also teach antibodies to the PRO269 polypeptide (see especially pages 108-111). The antibodies of Wood et al. inherently "specifically bind" the polypeptide of SEQ ID NO:96, since as noted previously antibody binding is determined by the variable regions structure and is necessarily "specific".

Wood et al. teach that forms of the antibodies include monoclonal (e.g., page 108, especially lines 32-33) and humanized (e.g., page 110, especially lines 1-16).

Wood et al. also teach antibody fragments (e.g. page 110, especially lines 11-12).

Finally, Wood et al. teach antibodies that are labeled (see e.g., page 112, especially lines 6-13).

Applicant is again reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antibodies.

The reference teachings thus anticipate the instant claimed invention.

The rejection is therefore maintained for the reasons of record in Paper No. 11.

16. Claims 39-43 are rejected under 35 U.S.C. 102(b) as being anticipated by Valenzuela et al. (WO 00/11015, see pages 1-2, 115-118, 167-168, 171-176, 183-184, 207-209 and pages 68-70 of the sequence listing, of record), as evidenced by the attached alignment "E" (of record).

Applicant's arguments, filed 3/31/03, have been fully considered but have not been found convincing.

Applicant' argues that the instant claims are entitled to an effective filing date of February 11, 2000.

For the reasons set forth supra, Applicant's argument with respect to the effective filing date of the instant claims has not been found convincing.

As previously noted, Valenzuela et al. teach an isolated vp15_1 polypeptide having 100% amino acid sequence identity to SEQ ID NO:96 as shown in Figure 36 of the instant application, as evidenced by the attached alignment.

Valenzuela et al. also teach antibodies to the vp15_1 polypeptide (see especially pages 207-209). The antibodies of Valenzuela et al. inherently "specifically bind" the polypeptide of SEQ ID NO:96, since as noted supra antibody binding is determined by the variable regions structure and is necessarily "specific".

Valenzuela et al. teach that forms of the antibodies include monoclonal and humanized antibodies (e.g., page 207, especially lines 29-33).

Valenzuela et al. also teach antibody fragments (e.g. page 208, especially lines 10-15).

Finally, Valenzuela et al. teach antibodies that are "diagnostic agents", therefore, Valenzuela et al. teach antibodies that are necessarily labeled either directly or indirectly to permit their detection (see e.g., page 208, especially lines 29-30).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitation of specific binding would be an inherent property of the referenced antibodies.

The reference teachings thus anticipate the instant claimed invention.

The rejection is therefore maintained for the reasons of record in Paper No. 11.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

18. Claims 39 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Valenzuela et al. (WO 00/11015, see pages 1-2, 115-118, 167-168, 171-176, 183-184, 207-209 and pages 68-70 of the sequence listing, of record), as evidenced by the attached alignment "E" (of record), in view of Ramakrishnan et al. (US Pat. No. 5,817,310, of record).

Applicant's arguments, filed 3/31/03, have been fully considered but have not been found convincing.

Applicant' argues that the instant claims are entitled to an effective filing date of February 11, 2000.

For the reasons set forth supra, Applicant's argument with respect to the effective filing date of the instant claims has not been found convincing.

As previously noted, the claims are drawn to an antibody that binds to the polypeptide of SEQ ID NO:96, wherein the antibody is labeled.

Valenzuela et al. have been discussed supra and teach an antibody that binds to the polypeptide of SEQ ID NO:96, wherein the antibody is a diagnostic agent.

Valenzuela et al. do not explicitly state that the antibody that is a diagnostic agent is a labeled antibody.

Ramakrishnan et al. teach that labeling of antibodies for use in various diagnostic applications (e.g., column 17, especially lines 1-33).

Therefore, it would have been obvious to the ordinary artisan at the time the invention was made to label the antibody of Valenzuela et al. using any of a number of art-recognized labels as taught by Ramakrishnan et al. The ordinary artisan would have been motivated to label the antibodies of Valenzuela et al. in order to provide a variety of detection agents that could be used in diagnostic assays as taught by Valenzuela et al. Given the art-recognized methods for labeling antibodies for diagnostic applications, as taught by Ramakrishnan, the ordinary artisan at the time the invention was made would clearly have had a reasonable expectation of producing label versions of the antibodies of Valenzuela et al. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The rejection is therefore maintained for the reasons of record in Paper No. 11.

Conclusion

19. No claim is allowed.

20. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3017.

Jessica Roark, Ph.D.
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June 16, 2003

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